

c2 27. (Amended) A composition as claimed in claim 1, wherein one-gram of licorice preparation or dried root is equivalent to 40 mg of glycyrrhizin.

REMARKS

I. Status of the claims

Claims 1-48 are pending. Claims 1-6, 9, 10 and 27 are examined on the merits. Claims 7, 8, 11-26 and 28-48 have been withdrawn from consideration pursuant to a restriction requirement. Applicants reserve the right to file one or more applications directed to that non-elected subject matter.

II. Amendments to the claims

Claim 1 has been amended to clarify that which is inherent in the meaning of an "effective amount" of *G. glabra* extract. As applicants have impressed throughout the examination of this application, an effective amount of *G. glabra* is an amount which is not therapeutically effective, *i.e.*, the *G. glabra* itself has negligible, if any, nutraceutical, antibiotic, antiinfectious or anticancerous properties. However, the effective amount of the *G. glabra* extract is effective in rendering the extract suitable as a **bio-enhancer** and/or **bioavailability facilitator**. Support for these amendments can be found throughout the specification. See, for example, page 4 of the specification, where applicants state: "[T]he main object of the invention is to provide novel compositions comprising extracts and compounds from the plant *Glycyrrhiza glabra* useful as a bioenhancer and capable of improving or enhancing the bio-availability of drugs such as antibiotics, anti-infective agents and of nutritional compounds."

Claim 27 also is proposed to be amended to clarify that one-gram of licorice preparation or dried root is equivalent to 40 mg of glycyrrhizin. See the paragraph bridging pages 9 and 10 of the present application for support for this amendment. This amendment was made in response to the examiner's rejection of December 18, 2001.

Applicants respectfully request entry of the proposed amendments and consideration of these amended claims.

III. Summary of the invention

The present invention uses a purified extract of *Glycyrrhiza glabra* to enhance the activities of drugs and compounds with which it is combined, as well as to improve the bioavailability of those substances to the cells, tissues and immune system of a treated individual. The inventors' surprising discovery was that even when used in amounts that render the *G. glabra* extract therapeutically ineffective (for example, ineffective as an antibacterial or antiviral agent), the effective amount of the *G. glabra* extract, in fact, boosts the activity of substances with which it is combined. The *G. glabra* extract of the present invention by itself is not therapeutic; it is not used to stimulate or induce any immune or biological pathway of the treated individual. The *G. glabra* extract is used to enhance the activity of a substance with which it is blended. It is *that* substance that invokes a biological response from the individual's body, not *G. glabra*.

III. Rejection of claim 27 under 35 U.S.C. § 112, second paragraph

In her Office Action of December 18, 2001, the examiner rejected claim 27 because "it is not clear" that one gram of licorice contains the equivalent of 40 mg of glycyrrhizin. The examiner kindly suggested at page 2 of the Office Action that "[I]f the language of the claim stated clearly that one gram of licorice is equivalent to 40 mg mg glycyrrhizin then the claim would be considered definite." Applicants, therefore, amend claim 27 to clarify this ratio, by reciting "wherein one-gram of licorice preparation or dried root is equivalent to 40 mg of glycyrrhizin." See the paragraph bridging pages 9 and 10 of the present application for support for this amendment. Accordingly, applicants request that the examiner enter the proposed amendment and withdraw the rejection.

IV. Rejection of the claims under 35 U.S.C. § 102(b)

The examiner also maintained that U.S. Patent Nos. 5,939,050 and 5,770,217 anticipated the present claims. According to the examiner's rationale, these prior art documents teach compositions comprising *G. glabra* in amounts that exert antimicrobial activity, (see the claims of the '050 patent), or as a dietary supplement because it stimulates T-cell activity and interferon activity and maintains normal blood and sugar levels (see column 5, lines 46-59 and the claims of the '217 patent).

(i) Claims 1-6 and 27 are not anticipated by either one of U.S. Patent Nos. 5,939,050 or 5,770,217

The examiner maintained her rejection of claims 1-5 and 27 as being allegedly anticipated by U.S. Patent No. 5,939,050, and claims 1-6 and 27 by U.S. Patent No. 5,770,217, under 35 U.S.C. § 102(b).

The examiner stated at page 3 of the Office Action that "US '050 clearly teaches a composition that contains *G. glabra* and an anti-infective agent. This composition is the same as the claimed composition. Therefore, since the compositions are the same, the composition taught by US '050 must have the same characteristics as the claimed composition if applicant's composition functions as claimed."

The examiner also asserted that "because the *G. glabra* extract of US '050 appears to be the same extract that is used by applicant" the extract of US '050 would, therefore, "contain the requisite amount of glycyrrhizin." See point 6, at page 3 of the Office Action.

Applicants respectfully disagree with the examiner's interpretation of the '050 patent and its alleged anticipatory disclosure, and traverse the rejection.

The '050 patent clearly states that the "oral hygiene product" of claim 1 comprises antimicrobial agent A and antimicrobial agent B in "an amount

effective to inhibit the growth of oral pathogenic bacteria." The claim further recites that an antimicrobial agent may be *G. glabra*.

Applicants state that the amount of *G. glabra* used in the present invention does not have anti-infective properties, such as antibacterial, antiviral or antimicrobial activities. Indeed, applicants illustrate, using a concentration of 1 µg/ml of glycyrrhizin, that in the presence of the compound, "no significant killing" of bacteria was observed. See "Examples" at page 14 of the present specification. Moreover, applicants show in Tables 8 and 9 at page 18 of the specification that even when 4 µg of glycyrrhizic acid was applied to a disc in the "disc diffusion assay" to measure the extent of antimicrobial properties of the *G. glabra* extract, the net zone of inhibition for *Mycobacterium smegmatis* and *Escherichia coli* was zero millimeters ("0 mm"). Thus, applicants show that even 4 µg of *G. glabra* extract does not reduce microbial growth. Nevertheless, that same amount of glycyrrhizic acid enhanced the net zone of inhibition (*i.e.*, microbial cell death) produced by rifampicin. See Tables 8 and 9.

Accordingly, the *G. glabra* extract of the present invention does not have antimicrobial activity but does enhance the antimicrobial activity of an antimicrobial agent or antibiotic, for example, with which it is combined.

With that understanding, it is clear that the '050 patent does not anticipate the present claims because the claims of the '050 patent require that the *G. glabra* be an antimicrobial agent. Thus, the '050 patent-holder states at column 5, lines 13-48, that "combinations of antimicrobial agents formed in accordance with the present invention exhibit a surprising and unexpectedly significant decrease" (emphasis added) in their minimal inhibitory concentrations. Indeed, Table 6 at column 11 of the '050 patent shows that 15.0 µg/ml of *G. glabra* alone is required to establish a minimal inhibitory concentration of *G. glabra* against *Actinomyces viscosus*. Similarly, 15.6 µg/ml of *G. glabra* is required to inhibit growth of *Porphyromonas gingivalis*. Both of these "MIC" values are reduced in the presence of one or more different antibiotics ("agents"). In contrast, the present application disclosed that a 1

µg/ml solution of *G. glabra*, while not antimicrobial itself, enhances the activity of a number of antibiotics.

Furthermore, the '050 patent states at the end of column 6 and at the beginning of column 7, that "the particular amount of antimicrobial agent present in compositions formed in accordance with the present invention is not limited to any particular value, provided that the amount present is effective at retarding the growth of bacteria and/or preventing the growth of bacteria" (emphasis added). The amount of *G. glabra* extract used in the present invention is not effective at retarding the growth of bacteria and/or preventing the growth of bacteria. The amount of *G. glabra* extract used in the present invention is effective in enhancing the activity of *another* antimicrobial agent. For these reasons, applicants contend that in no way does the '050 patent anticipate the present claims.

Similarly, the present claims are not anticipated by the '217 patent. That patent-holder states at column 3, lines 50-57, that the disclosed herbs and herbal extracts, "when consumed in the combinations described herein, have enhanced beneficial effects regarding immune enhancement, maintenance of normal hematologic characteristics and maintenance of body weight through appetite enhancement." Indeed, in that light, the patent-holder elaborates that powdered *G. glabra* is known to stimulate "T-cell activity and interferon production and to reduce inflammation and fatigue through its content of glycyrrhizic acid which results in increased glucocorticoid and mineralocorticoid activity. It is effective in healing duodenal ulcers and has a much lower reoccurrence rate. It has exhibited significant antiviral activity against Hepatitis B, Epstein-Barr virus and Cytomegalovirus. It maintains normal blood pressure and sugar levels."

Thus, the dietary supplement of claims 1 and 7 of the '217 patent recite a percentage of dry weight of *G. glabra* that possesses these properties as being "0.25-5%" of the final supplement composition. However, the recommended

amount of *G. glabra* extract used in the present invention is below that which would, by itself, exhibit the properties taught by the '217 patent.

Furthermore, the examiner has not met the burden of showing that the amount of *G. glabra* disclosed in the '217 patent inherently possesses a non-therapeutic effect as prescribed by the present invention. Indeed, the skilled artisan, having read the '217 patent, would expect that 0.25-5% represents a sufficient quantity of *G. glabra* in the final dietary supplement to exert the beneficial physiological, immunological and biological effects described in column 3 of that patent. Nowhere does the '217 patent suggest that the dietary supplement comprise *G. glabra* in amounts that are ineffective in eliciting the desired effects upon the consumer.

It is well settled that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). The cited references must disclose each and every element of the claimed invention and the "identical invention must be shown in as complete detail as is contained in the ... claim," *Richardson v. Suzuki Motor Co.* 868 F.2d, 1226, 1236 (Fed. Cir. 1989). Neither the '050 patent nor the '217 patent disclose each and every element of the claimed invention. That is, the cited prior art do not disclose or suggest a composition comprising *G. glabra* in an amount that renders the *G. glabra* **ineffective** as an antimicrobial substance, but **effective** as a bio-enhancer for boosting the properties of another antimicrobial agent and as a bioavailability facilitator. Accordingly, the present claims are not anticipated by any one of the prior art documents cited in the Office Action. Applicants therefore respectfully request that the examiner withdraw these rejections.

VI. Rejection of the claims under 35 U.S.C. § 103(a)

The examiner contended that the present claims are obvious in light of the '217 patent because "an artisan of ordinary skill would still be motivated to optimize the composition taught by US '217," since it is "well known that an amount of an ingredient can be modified to determine the most effective combination of elements."

The examiner further alleged that the present claims are obvious over U.S. Patent Nos. 5,939,050 and 5,478,829 and The Merck Index. She believed that "the *G. glabra* extract of US '050 is the same as the *G. glabra* extract claimed by applicant," and that, therefore, "a person of ordinary skill in the art would be motivated to combine a *G. glabra* extract with other antibacterial agents."

Applicants respectfully disagree and traverse the rejection.

VII. The present claims are not obvious over the cited prior art

At the outset, none of the cited prior art documents teaches that a therapeutically *ineffective* amount of *G. glabra* can be used to enhance the antimicrobial properties of other substances with which it is combined. Further, there is no guidance in any of the cited art documents for determining what amount of *G. glabra* has little or negligible effect upon killing or retarding the growth of microbes. Rather, the converse is true in both respects. The prior art teaches amounts of *G. glabra*, in combination with other antimicrobial agents, **that is required to inhibit pathogenic growth**. Indeed, none of the cited art teaches that lowering the amount of *G. glabra* to levels where it has negligible therapeutic effect by itself is a beneficial way in which the activity of other antimicrobial agents can be enhanced.

Accordingly, there is no suggestion or motivation to lower the amount of *G. glabra* so that it is therapeutically ineffective as recited in the present claims. **The prior art teaches the therapeutically beneficial reasons why *G. glabra* is included in their final compositions**. They do not teach that the *absence* of

these therapeutic effects is beneficial, as do applicants in the present application.

The examiner acknowledged, at page 5 of the Office Action, that the *G. glabra* used in the present invention "is not used as an antibacterial agent" but goes on to state that "however, US '050 clearly teaches that *G. glabra* extracts are antibacterial agents." According to the examiner, this means that one would be "motivated to combine a *G. glabra* extract with other antibacterial agents."

Applicants respectfully point out that the examiner's conclusion is incorrect. She is right that the present invention does not use *G. glabra* as an antibacterial agent and that the '050 patent does use *G. glabra* as an antibacterial agent, but only at amounts sufficient to exert those antibacterial properties. Accordingly, one would not be motivated, after reading the '050 patent, to seek concentrations of *G. glabra* that would not produce the antibacterial effects desired in that patent. Therefore, there is no motivation to use *G. glabra* at low amounts as taught by the instant application.

VIII. Conclusion

It is respectfully urged that upon entry of the proposed amendments, the examined claims are now in condition for allowance. Early notice to that effect is earnestly solicited.

The examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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MARKED-UP VERSION OF THE CLAIMS FILED JUNE 18, 2002

1. (Amended) A composition comprising (i) an effective amount of an extract or compound obtained from the plant *Glycyrrhiza glabra* and (ii) a therapeutically effective amount of one or more nutraceuticals, antibiotics, anti-infective agents and anti-cancer agents, wherein said effective amount of said extract or said compound is insufficient for said extract by itself or said compound by itself to be a therapeutically effective nutraceutical, antibiotic, anti-infective agent or anti-cancer agent, and wherein said extract or said compound is effective as a bio-enhancer and bioavailability facilitator [useful as a bio-enhancer and bioavailability facilitator together with a therapeutically effective amount of one or more nutraceuticals, antibiotics, anti-infective agents and anti-cancer agents].

27. (Amended) A composition as claimed in claim 1, wherein one-gram of licorice preparation or dried root is equivalent to 40 mg of glycyrrhizin [licorice preparation or dried root is given as one-gram equivalent to 40 mg of glycyrrhizin].